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POLYGLYCEROLS AND POLYGLYCEROL ESTERS IN NUTRITION, HEALTH AND DISEASE

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Polyglycerols and polyglycerol esters, as a broad class of compounds, have been used for a number of years as useful and desirable adjuncts in nutrition, health, and in the treatment of certain diseases. The use of these compounds has been limited by their lack of quality and reproducibility in nutritional and medical products that would be submitted for approval to the Food & Drug Administration (FDA). With the process developed by Babayan and issued as U.S. Patent No. 3,637,774[1], this limitation was overcome. In recent years we have noted the availability of such products and the approval by the FDA and the Codex Alimentarius for the use of polyglycerol esters of fatty acids in foods.

The edible and industrial applications of the various polyglycerol esters are appearing in the literature, as well as products which list polyglycerol esters as one of the components in the formulation of the product. It is not surprising that a broad range class of compounds having multi-functionality and flexibility is being considered over an equally broad range of hydrophilic-lipophilic emulsification requirements. A study of their physical and chemical composition and properties is indicative of their unique and useful functionality and applications.

Although in previous presentations and publications[2-12] we have covered the salient characteristics of the polyglycerol esters, it may be useful to briefly summarize the data for the completeness of this presentation.

When glycerine is subjected to heat in the presence of a catalyst, polymerization takes place. Usually the condensation takes place at temperatures above 200°C with the elimination of water and the formation of an ether linkage between two glycerine molecules. Fig. 1 illustrates this reaction. The condensation reaction involves the α-hydroxyl groups of the glycerol molecule. Subsequent polymerization proceeds with the remaining α-hydroxyl groups and another glycerol molecule to form higher polymers. The reaction under these conditions appears to be linear and a range of polymers can be formed. The reaction can be followed by the amount of water that is formed from the polymerization as well as the changes in refractive index, viscosity and hydroxyl value of the product. Some typical specific gravity and viscosity figures for a range of the polyglycerols is given in Table 1. The polyglycerols of the various polymer ranges are viscous fluids which are water soluble.

The polyglycerols may be converted into polyglycerol esters by direct esterification with a fatty acid or by intermolecular rearrangement with a triglyceride. The polyglycerol formed by the heat polymerization can now be reacted with fatty acids of varying chain length and unsaturation. Fatty acids

TABLE 1. Typical Viscosities and Specific Gravities of Commercially Prepared Polyglycerols

Polyglycerol	Specific gravity	Viscosity, cs. 65.6°	Viscosity, cs. 99°C
Triglycerol	1.279	640	70
Hexaglycerol	1.283	1700	110
Decaglycerol	1.290	3200	280

from acetic to tetracosencic in the saturated series and/or mono, di and polyunsaturated fatty acids such as oleic, linoleic and linolenic, etc. in the unsaturated series may be used in the direct esterification. The other alternative is to conduct molecular rearrangement with a triglyceride of known composition and structure a new polyglycerol ester at random distribution. Fig. 2 illustrates the two reactions that may be used in the preparation of the polyglycerol esters. Depending upon the molar ratios used in the reaction and the condition employed, one is able to prepare partial or neutral esters of a polyglycerol of a given molecular weight and fatty acids and/or triglycerides of known composition. The polyglycerol esters prepared by these approaches constitute the basis for the diversified products that are available for edible, medical and industrial uses. R.T. McIntyre summarized the reactions and their product characteristics recently in an update on the polyglycerol esters[13]. The effect of the fatty acid chain length and degree of esterification on the hydrophilic-lipophilic balance (HLB) values of the polyglycerol esters is illustrated in Figs. 3, 4 & 5. The range of their specific gravities is given in Fig. 7. Their hydrophilic-lipophilic ranges is illustrated in Table 2. The wide range of the polyglycerol esters is clearly indicated in these figures and tables and once again re-emphasizes the flexibility and utility of the class as a whole.

Concurrently with the edible and industrial applications and uses of the polyglycerol esters, several pharmaceutical, medical, nutritional and dietetic groups have been exploring the unique characteristics of the polyglycerol esters.

Since the polyglycerols are water soluble compounds and their viscosity increases with the increase in molecular weight, they become useful components in viscosity control, gravity control and humectants able to carry water and yet maintain the desired consistency of the food or medical formulation.

TABLE 2. HLB Values Calculated from the Theoretical Compositions of Products Formed by Reaction of Stearic Acid with Polyglycerols

Polyglycerol	HLB — Molar Ratio of Stearic Acid : Polyol 1:1	2:1	4:1
Triglycerol	6.7 (8.8)	4.9 (5.3)	2.6 (2.6)
Hexaglycerol	10.1 (12.2)	8.1 (8.8)	5.1 (5.1)
Decaglycerol	12.5 (14.5)	10.6 (11.2)	7.5 (7.5)

The partial esters of polyglycerols can be aerators or defoamers, emulsifiers, clouding agents, weighting agents and solvents for a variety of food product compositions. They tend to be multi-functional and do the work of several other additives.

The U.S. Patent No. 4,093,750[14], demonstrates the suitability of such polyglycerol esters in the preparation of beverages. The multifunctional polyglycerol esters not only behave as solvents and carriers for flavoring agents, but also as emulsifiers and clouding agents in such beverage preparations. Depending on the type of beverage desired, one can select the particular polyglycerol ester to bring out the desired characteristics.

The neutral esters of polyglycerols can be polymeric fats, lubricants, crystallization inhibitors, gloss additives, and moisture barrier agents, as well as solvents and carriers for oil soluble vitamins, colors and steroids.

The ability of polyglycerols and polyglycerol esters to replace fat in foods and yet maintain the satiety and feeling of eating rich fatty foods has been utilized in special dietetic products, where more than 50% of the calories have been eliminated without sacrificing the consistency, appearance, and taste of the food. For example, the Weight Watchers imitation ice cream and dietetic dessert contains no fat, but uses the polyglycerol esters to give satiety and to reduce the caloric content of the food.

Aside from the unique characteristic of being able to replace or eliminate fat from a formula, the polyglycerol esters also tend to reduce the actual caloric metabolic yield of a food. If we assume that the entire molecule of the polyglycerol mono-ester of a fatty acid is completely metabolized, a decaglycerol mono-ester for example, would contribute 6-6.5 kcal/g in contrast to the 9.2 kcal/g for fats. If, however, the polyglycerol backbone is not metabolized and only the fatty acid moiety is utilized, then the same compound would have less than 2 kcal/g. Fig. 8 illustrates the two cleavage points which are in question in the metabolic fate of the polyglycerols and polyglycerol esters. Our data has indicated that the polyglycerols and polyglycerol esters are quantitatively metabolized and utilized in both animal and human studies[16]. Several other investigators, primarily Michaels and Coots[17], have argued that the polyglycerol backbone is not completely metabolized. Using the largest polyglycerol molecule allowed by FDA, as the sole source of fat, decaglycerol was found in the urine of the test animals. As yet we do not know whether this finding represents excesses or the non-metabolized portion. In any event, all products appeared to be non-toxic.

The medical and pharmaceutical applications of the polyglycerols and the polyglycerol esters are an extension of the edible applications of these compounds, where the same multi-functional characteristics can be utilized in medical formulations. In addition to their uses as emulsifiers, solvents, and carriers for medications, the polyglycerol esters have demonstrated their unique solvancy for carrying lipids in various metabolic applications[18]. In a conversation with W.G. Linscheer, MD (April 1981) the polyglycerol esters have acted as substitutes or as having a sparing action for patients with pancreatic insufficiency and bile acid insufficiency.

The medical and pharmaceutical applications of the polyglycerols and

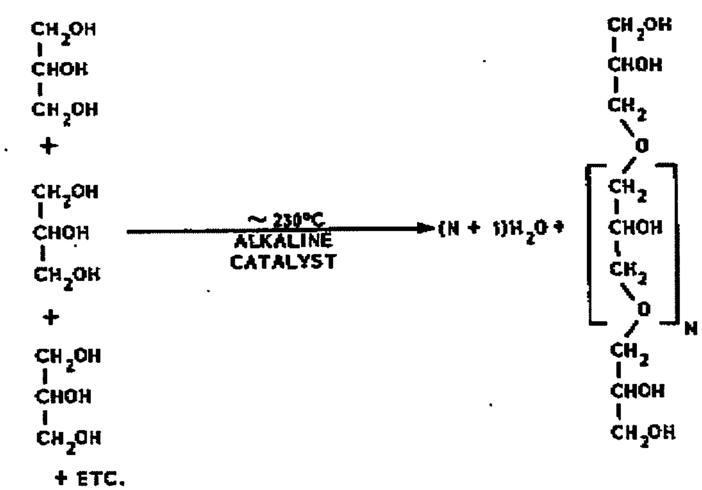


FIGURE 1. Preparation of polyglycerols.

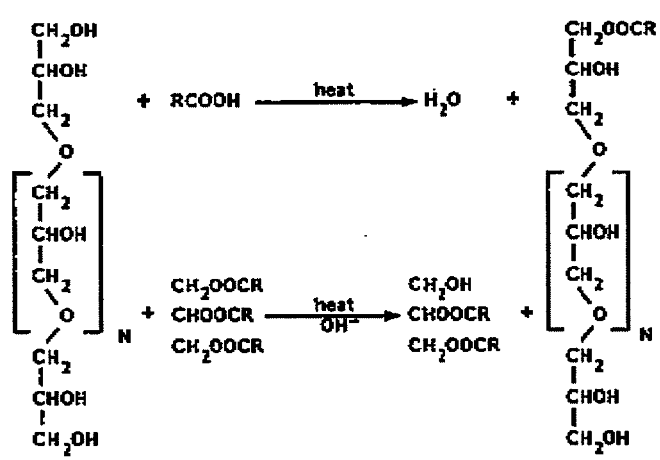


FIGURE 2. Partial ester formation.

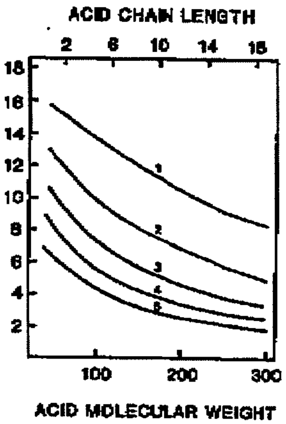


FIGURE 3. Effect of fatty acid chain length and degree of esterification on the HLB of triglycerol esters.

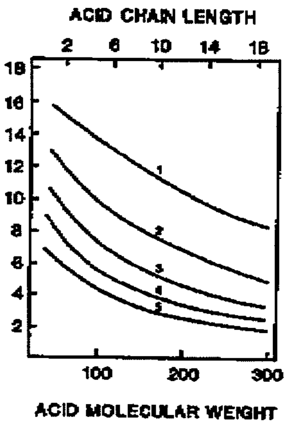


FIGURE 4. Effect of fatty acid chain length and degree of esterification on the HLB of decaglycerol esters.

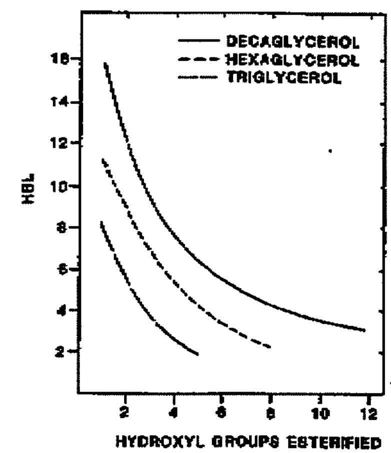


FIGURE 5. HLB ranges covered by stearic acid esters of triglycerol, hexaglycerol and decaglycerol.

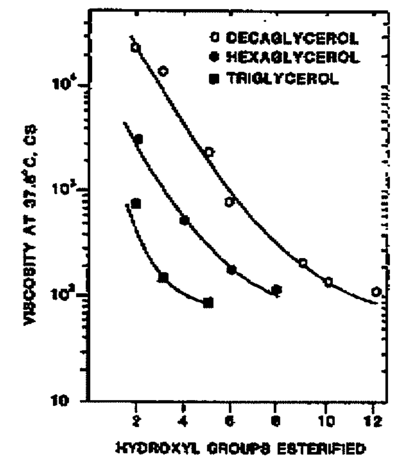


FIGURE 6. Viscosity of polyglycerol esters.

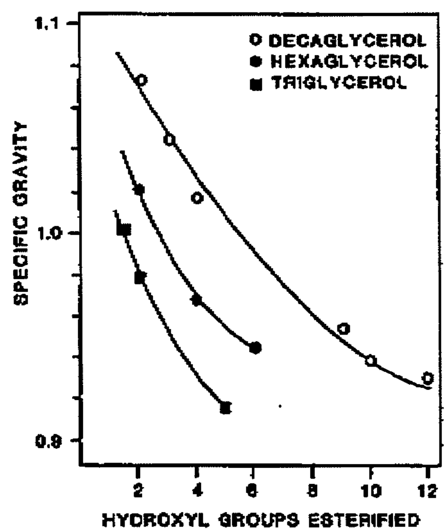
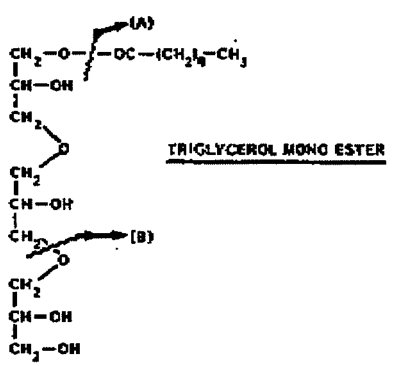


FIGURE 7. Specific gravity of polyglycerol esters.



(A): CLEAVAGE AT THE ESTER SITE IS WELL DOCUMENTED

(B): CLEAVAGE AT THE ETHER SITE IS NOT WELL DOCUMENTED. AND IS STILL CONTROVERSIAL. UNDER LABORATORY CONDITIONS ETHER LINKAGES REQUIRE DRASTIC BOILING WITH HBr OR HI TO AFFECT CLEAVAGE. ENZYMATIC CLEAVAGE MAY EXIST BUT HAS NOT BEEN DOCUMENTED. MICHAEL & COOTS (1971) SHOWED THAT THE POLYGLYCEROL MOIETY IS EXCRETED WITHOUT BEING METABOLIZED AS AN ENERGY SOURCE.

FIGURE 8. Possible modes of cleavage of polyglycerols and polyglycerol esters during metabolism in a living system.

polyglycerol esters are practically in their infancy. What has been done thus far is merely the extension of the edible applications. The future will see the polyglycerols and polyglycerol esters making a marked penetration into the medical, pharmaceutical and health care field because of their versatility and unique physical and chemical characteristics, which can be programed at will to give the specific functionality desired.

Polyglycerols and polyglycerol ester applications and uses in the medical, health and disease areas were a natural extension of the knowledge we had acquired in the edible and industrial applications.

Grundy and Ahrens and others have used polyglycerol esters, notably the tri and hexaglycerol oleates, as emulsifiers in special diets to solubilize and emulsify fat and cholesterol[19]. Such emulsions have proven to be very satisfactory in carrying the fat and cholesterol in a uniform and stable state. The polyglycerol esters have been suggested to the pharmaceutical field as a unique class of emulsifiers, which are suitable for emulsion preparations where fat, cholesterol or other medication is to be solubilized and/or carried. The oleates are liquid and the stearates are solid. Depending upon the type of product involved, one can select the specific polyglycerol ester best suited for the functionality. For example, the oleates are good solvents for cholestrol and other steroids and ring compounds. The stearates are good aerating agents and best suited for creams and ointments where aeration and volume is desired.

Kabara and co-workers in a series of publications have shown that the polyglycerol laurates have anti-microbial properties[20-24]. Such anti-microbial properties are at an optimum with lauric acid and fall of on either side of the fatty acid chain length. The anti-microbial properties of the polyglycerol laurates progressively increase as the molecular weight of the polyglycerol increases. Thus, tri, hexa and decaglycerol laurates show progressive greater anti-microbial power. The number of free hydroxyls apparently enhances the anti-microbial ability of the laurate ester.

In this connection the recent data that is beginning to be reported in the literature appears to point to the excess of the production of bile acids and their contact with colon tissues over prolonged periods of time. This increased exposure appears to increase the incidence of colonic cancer. Particularly in diets rich in fat, especially polyunsaturated fat, the incidences appear to be greater than that with diets having low fat content. If the polyglycerol esters can serve as a bile acid replacement and/or a sparing action, then they may be able to reduce the need for excessive bile acid production and the excessive concentrations appearing in the intestinal tract. Certainly the alternatives to the production and presence of high concentrations of bile acid in the colon should be helpful in reducing the instances of colonic cancer. We shall wait to see whether polyglycerol esters can play a useful role in this area.

This good solvent characteristic of the polyglycerol oleates for cholesterol has prompted some investigators to consider them not only as carriers and solvents for cholesterol, but also as possible agents for regression and solubilizer of atheromas and plaque regression. W.G. Linscheer, MD and others (April 1981) have found polyglycerol esters, notably and triglycerol monocaprylate and oleate, to increase fatty acid transport through the intestinal wall, markedly enhancing fat utilization in patients requiring fat or calorie sup-

plementation. Linscheer also found that in patients deficient in or devoid of bile acids and/or pancreatic lipase, the polyglycerol esters were able to alleviate and/or show sparing action for these substances. The possibility that polyglycerol esters may possibly substitute bile acids and pancreatic lipase, suggests a number of areas of medical application, but much more clinical evidence is needed before we can arrive at a decision. The presence of polyglycerol esters in food products, however, may prove to be very helpful to patients having such deficiencies in bile acid and pancreatic lipase secretions.

In a conversation S.A. Hashim, J. Saleh and others (December 1980) have noted the beneficial effect of polyglycerol esters, notably the triglycerol mono-caprylate and the deca-glycerol mono-laurate in the absorption and transport mechanism in humans. In some ways their work is collaborative to that carried out by Linscheer and extends the area of utilization of the polyglycerol esters. Hopefully other experimental data will become available to confirm other such unique uses of the polyglycerol esters.

The anti-microbial, emulsification and solvent action of polyglycerol caprylates and laurates presents the possibility that such products can be considered as emulsifiers and protective agents for intravenous preparations, where sterility and protection against bacterial infection is always a desired state. Alone or with egg phosphatides, such polyglycerol laurates may well serve to improve present parenteral fat emulsions.

In the area of dietetic formulations where caloric restriction is required, the polyglycerol esters can serve as hybrid fats or as low calorie food product. Kaunitz and Babayan demonstrated that polyglycerol esters are safe and non-toxic, even when used as the sole source of fat in a balanced diet. Babayan has postulated that such polyglycerol esters can play the role of a dietetic fat not only because the caloric value of the polyglycerol mono-esters are in the range of 6-6.5 calories, but also because one can formulate products devoid of fat or very low level of fat, and yet give the impression that one is eating a rich fatty food[8]. The palatability and satiety factor of such products is very acceptable.

Some questions have been raised by Michael and Coots whether the polyglycerol backbone is metabolized. Our data submitted to the FDA, for the clearance of such products in food use, showed that polyglycerols are completely metabolized. In the event, however, that the contention of Michael and Coots proves to be valid, such polyglycerol mono-esters would have less than 2 calories/g instead of 6-6.5 calories/g. Thus, these low calorie emulsifiers would be even better suited for low calorie dietetic foods.

All in all, the polyglycerol esters for consideration as a medical and physiological tool, as well as a nutritional and dietetic food component promises to be a very fruitful area of investigation and development. It remains for the physicians, clinicians, and dietitians to increase our knowledge with their investigative results.

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